

**AMENDMENTS TO THE CLAIMS:**

This listing of the claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

1-24 (canceled)

25. (Currently amended) A cell expressing a multivalent composition for active idiotype immunotherapy produced according to a method comprising:

- a) providing:
  - i) malignant B cells isolated from a patient having a quasi-clonal B-cell lymphoma;
  - ii) at least one expression vector;
  - iii) an amplification vector comprising a recombinant oligonucleotide having a sequence encoding a first inhibitible enzyme operably linked to a heterologous promoter; and
  - iv) a T lymphoid parent cell line;
- b) isolating nucleic acid from said malignant cells, said nucleic acid comprising nucleotide sequences selected from the group consisting of nucleotide sequences encoding at least one  $V_H$  region and at least two  $V_L$  regions, nucleotide sequences encoding at least two  $V_H$  regions and at least one  $V_L$  region, and nucleotide sequences encoding at least two  $V_H$  regions and at least two  $V_L$  regions, wherein said at least two  $V_L$  regions differ by at least one idiotope, wherein said at least two  $V_H$  regions differ by at least one idiotope, and wherein said  $V_H$  and  $V_L$  regions are derived from immunoglobulin molecules expressed by said malignant cells;
- c) inserting said nucleic acid comprising nucleotide sequences encoding said  $V_H$  and  $V_L$  regions into said at least one expression vector ;
- d) introducing said at least one expression vector and said amplification vector into said parent cell line to generate one or more transformed cells;

e) growing said transformed cells in a first aqueous solution containing an inhibitor capable of inhibiting said first inhibitable enzyme wherein the concentration of said inhibitor present in said first aqueous solution is sufficient to prevent growth of said parent cell line; and

f) identifying a transformed cell capable of growth in said first aqueous solution, wherein said transformed cell capable of growth expresses a combination of  $V_H$  and  $V_L$  regions selected from the group consisting of at least one  $V_H$  region and at least two  $V_L$  regions, at least two  $V_H$  regions and at least one  $V_L$  region, and at least two  $V_H$  regions and at least two  $V_L$  regions, wherein said at least two  $V_L$  regions differ by at least one idiotope, wherein said at least two  $V_H$  regions differ by at least one idiotope, and wherein said  $V_H$  and  $V_L$  regions comprise a protein molecule,

wherein said multivalent composition comprises said expressed  $V_H$  and  $V_L$  regions.

26. (Previously presented) The composition of Claim 25, wherein nucleotide sequences encoding said  $V_H$  and  $V_L$  regions comprise at least two  $V_H$  and at least one  $V_L$  regions.

27. (Previously presented) The composition of Claim 25, wherein nucleotide sequences encoding said  $V_H$  and  $V_L$  regions comprise at least one  $V_H$  and at least two  $V_L$  regions.

28. (Currently amended) A cell expressing a multivalent composition for active idiotype immunotherapy produced according to a method comprising:

- a) providing:
  - i) malignant B cells isolated from a patient having a quasi-clonal B-cell lymphoma;
  - ii) at least one expression vector;
  - iii) an amplification vector comprising a first recombinant oligonucleotide having a sequence encoding a first

- inhibitible enzyme operably linked to a heterologous promoter;
- iv) a selection vector comprising a second recombinant oligonucleotide having a sequence which encodes a selectable gene product; and
- v) a T lymphoid parent cell line;
- b) isolating nucleic acid from said malignant cells, said nucleic acid comprising nucleotide sequences selected from the group consisting of nucleotide sequences encoding at least one  $V_H$  region and at least two  $V_L$  regions, nucleotide sequences encoding at least two  $V_H$  regions and at least one  $V_L$  region, and nucleotide sequences encoding at least two  $V_H$  regions and at least two  $V_L$  regions, wherein said at least two  $V_L$  regions differ by at least one idiotope, wherein said at least two  $V_H$  regions differ by at least one idiotope, and wherein said  $V_H$  and  $V_L$  regions are derived from immunoglobulin molecules expressed by said malignant cells;
- c) inserting said nucleic acid comprising said nucleotide sequences encoding said  $V_H$  and  $V_L$  regions into said at least one expression vector;
- d) introducing said at least one expression vector, said amplification vector and said selection vector into said parent cell line to generate transformed cells;
- e) introducing said transformed cells into a first aqueous solution, said first aqueous solution requiring the expression of said selectable gene product for growth of said transformed cells;
- f) identifying at least one transformed cell capable of growth in said first aqueous solution;
- g) introducing said transformed cell capable of growth in said first aqueous solution into a second aqueous solution, said second aqueous solution comprising an inhibitor capable of inhibiting said first inhibitible enzyme, wherein the concentration of said inhibitor present in said second aqueous solution is sufficient to prevent growth of said parent cell line; and
- h) identifying at least one transformed cell capable of growth in said second aqueous solution, wherein said transformed cell capable of growth expresses a combination of  $V_H$  and  $V_L$  regions selected from the group consisting of at least one  $V_H$

region and at least two  $V_L$  regions, at least two  $V_H$  regions and at least one  $V_L$  region, and at least two  $V_H$  regions and at least two  $V_L$  regions, wherein said at least two  $V_L$  regions differ by at least one idiotope, wherein said at least two  $V_H$  regions differ by at least one idiotope, and wherein said  $V_H$  and  $V_L$  regions comprise a protein molecule,

wherein said multivalent composition comprises said expressed  $V_H$  and  $V_L$  regions.

29. (Currently amended) A clone expressing a multivalent composition for active idiotype immunotherapy produced according to a method comprising:

- a) providing:
  - i) malignant B cells isolated from a patient having a quasi-clonal B-cell lymphoma;
  - ii) at least one expression vector;
  - iii) an amplification vector comprising a first recombinant oligonucleotide having a sequence encoding a first inhibitible enzyme operably linked to a heterologous promoter;
  - iv) a selection vector comprising a second recombinant oligonucleotide having a sequence which encodes a selectable gene product; and
  - v) a T lymphoid parent cell line;
- b) isolating nucleic acid from said malignant cells, said nucleic acid comprising nucleotide sequences selected from the group consisting of nucleotide sequences encoding at least one  $V_H$  region and at least two  $V_L$  regions, nucleotide sequences encoding at least two  $V_H$  regions and at least one  $V_L$  region, and nucleotide sequences encoding at least two  $V_H$  regions and at least two  $V_L$  regions, wherein said at least two  $V_L$  regions differ by at least one idiotope, wherein said at least two  $V_H$  regions differ by at least one idiotope, and wherein said  $V_H$  and  $V_L$  regions are derived from immunoglobulin molecules expressed by said malignant cells;
- c) inserting said nucleic acid comprising said nucleotide sequences encoding said  $V_H$  and  $V_L$  regions into said at least one expression vector;

- d) introducing said at least one expression vector, said amplification vector and said selection vector into said parent cell line to generate transformed cells;
- e) introducing said transformed cells into a first aqueous solution, said first aqueous solution requiring the expression of said selectable gene product for growth of said transformed cells;
- f) identifying at least one individual clone of transformed cells capable of growth in said first aqueous solution;
- g) introducing said individual clone capable of growth in said first aqueous solution into a second aqueous solution, said second aqueous solution comprising an inhibitor capable of inhibiting said first inhibitable enzyme, wherein the concentration of said inhibitor present in said first aqueous solution is sufficient to prevent growth of said parent cell line; and
- h) identifying at least one individual clone capable of growth in said second aqueous solution, wherein said clone capable of growth expresses a combination of  $V_H$  and  $V_L$  regions selected from the group consisting of at least one  $V_H$  region and at least two  $V_L$  regions, at least two  $V_H$  regions and at least one  $V_L$  region, and at least two  $V_H$  regions and at least two  $V_L$  regions, wherein said at least two  $V_L$  regions differ by at least one idiotope, wherein said at least two  $V_H$  regions differ by at least one idiotope, wherein said  $V_H$  and  $V_L$  regions comprise a protein molecule,

wherein said multivalent composition comprises said expressed  $V_H$  and  $V_L$  regions.

30-32 (canceled)